



06-10-0

#20

CPA/1600

**CONTINUED PROSECUTION APPLICATION (CPA)
REQUEST TRANSMITTAL**

Submit an original, and a duplicate for fee processing.
(Only for Continuation or Divisional applications under 37 CFR 1.53(d))

CHECK BOX, if applicable:
 DUPLICATE

Address to:	Attorney Docket No. of Prior Application	201487/1030 (SEN-002PCT-US)
Mail Stop CPA Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	First Named Inventor	Karube
	Examiner Name	Bronwen M. Loe
	Group Art Unit	1636
	Express Mail Label No.	EV139569351US

This is a request for a continuation or divisional application under 37 CFR 1.53(d), (continued prosecution application (CPA)) of prior application number 09 / 623,970, filed on March 12, 1999, entitled Site-Specific Cell Perforation Technique.

NOTES

FILING QUALIFICATIONS: The prior application identified above must be a nonprovisional application that is either: (1) complete as defined by 37 CFR 1.51(b), or (2) the national stage of an international application in compliance with 35 U.S.C. 371. Effective May 29, 2000, a CPA may only be filed in a utility or a plant application if the prior nonprovisional application was filed before May 29, 2000. A CPA may be filed in a design application regardless of the filing date of the prior application. See "Request for Continued Examination Practice changes to and Provisional Application Practice," Final Rule, 65 Fed. Reg. 50092 (Aug. 16, 2000); Interim Rule, 65 Fed. Reg. 14865 (Mar. 20, 2000), 1233 Off. Gaz. Pat. Office (Apr. 11, 2000).

C-I-P NOT PERMITTED: A continuation-in-part application cannot be filed as a CPA under 37 CFR 1.53(d), but must be filed under 37 CFR 1.53(b).

EXPRESS ABANDONMENT OF PRIOR APPLICATION: The filing of this CPA is a request to expressly abandon the prior application as of the filing date of the request for a CPA. 37 CFR 1.53(b) must be used to file a continuation, divisional, or continuation-in-part of an application that is not to be abandoned.

ACCESS TO PRIOR APPLICATION: The filing of this CPA will be construed to include a waiver of confidentiality by the applicant under 35 U.S.C. 122 to the extent that any member of the public who is entitled under the provisions of 37 CFR 1.14 to access to, copies of, or information concerning, the prior application may be given similar access to, copies of, or similar information concerning, the other application or applications in the file jacket.

35 U.S.C. 120 STATEMENT: In a CPA, no reference to the prior application is needed in the first sentence of the specification and none should be submitted. If a sentence referencing the prior application is submitted, it will not be entered. A request for a CPA is the specific reference required by 35 U.S.C. 120 and to every application assigned the application number identified in such request, 37 CFR 1.78(a).

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provided credit card information and authorization on PTO-2038.

1. Enter the unentered amendment previously filed on _____ under 37 CFR 1.116 in the prior nonprovisional application.
2. A preliminary amendment is enclosed.
3. This application is filed by fewer than all the inventors named in the prior application, 37 CFR 1.53(d)(4).
 - a. **DELETE** the following inventor(s) named in the prior nonprovisional application:

b. The inventor(s) to be deleted are set forth on a separate sheet attached hereto.
4. A new power of attorney or authorization of agent (PTO/SB/81) is enclosed.
5. Information Disclosure Statement (IDS) is enclosed:
 - a. PTO-1449
 - b. Copies of IDS Citations

06/11/2003 MAHMED1 00000117 09623970

01 FC:2006

375.00 OP

CLAIMS	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
	TOTAL CLAIMS (37 CFR 1.16(c) or (j))	20 - 20* =	0	x \$ =	0
	INDEPENDENT CLAIMS (37 CFR 1.16(b) or (i))	2 - 3** =	0	x \$ =	0
	MULTIPLE DEPENDENT CLAIMS (if applicable) (37 CFR 1.16(d))			+ \$ =	
				BASIC FEE (37 CFR 1.16)	375
			Total of above Calculations =		375
	Reduction by 50% for filing by small entity (Note 37 CFR 1.27).				
	* Reissue claims in excess of 20 and over original patent. ** Reissue independent claims over original patent.			TOTAL =	

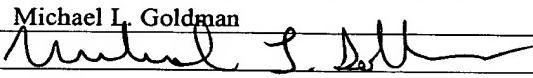
6. Small entity status: Applicant claims small entity status. See 37 CFR 1.27.
7. The Commissioner is hereby authorized to credit overpayments or charge the following fees to Deposit Account No. 14-1138:
- Fees required under 37 CFR 1.16.
 - Fees required under 37 CFR 1.17.
 - Fees required under 37 CFR 1.18.
8. A check to cover the \$375.00 filing fee is enclosed.
9. Payment by credit card. Form PTO-2038 is attached.
10. Applicant requests suspension of action under 37 CFR 1.103(b) for a period of _____ months (not to exceed 3 months) and the fee under 37 CFR 1.17(i) is enclosed.
11. New Attorney Docket Number, if desired
[Prior application Attorney Docket Number will carryover to this CPA unless a new Attorney Docket Number has been provided herein.]
12. a. Receipt For Facsimile Transmitted CPA (PTO/SB/29A)
b. Return Receipt Postcard (Should be specifically itemized, See MPEP 503)
13. Other: Second Request for Corrected Filing Receipt (w/attach.)

NOTE: The prior application's correspondence address will carry over to this CPA UNLESS a new correspondence address is provided below.

14. NEW CORRESPONDENCE ADDRESS

<input type="checkbox"/> Customer Number of Bar Code Label	(insert Customer No. or Attach bar code label here)			or <input checked="" type="checkbox"/> New correspondence address below		
Name	Nixon Peabody LLP					
Address	Clinton Square, P.O. Box 31051					
City	Rochester	State	NY	Zip Code	14603-1051	
Country	USA	Telephone	(585) 263-1304	Fax	(585) 263-1600	

15. SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Name (Print/Type)	Michael L. Goldman
Signature	
Registration No. (Attorney/Agent)	30,727
Date	June 9, 2005



EXPRESS MAIL CERTIFICATE

DOCKET NO.: **201487/1030 (SEN-002PCT-US)**

APPLICANT: **Karube et al.**

TITLE: **SITE-SPECIFIC CELL PERFORATION TECHNIQUE**

Certificate is attached to the **Fee Transmittal for FY 2003 (1 page)** of the above-named application.

EXPRESS MAIL NUMBER: **EV139569351US**

DATE OF DEPOSIT: **June 9, 2003**

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Mail Stop CPA, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450..

Cheryl Sanders
**(Typed or printed name of person
mailing paper or fee)**

Cheryl Sanders
**(Signature of person mailing paper
or fee)**

JUN 09 2003

FEE TRANSMITTAL FOR FY 2003

Patent fees are subject to annual revision.

 Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$1,360)

Complete if Known

Application Number	CPA of 09/623,970
Filing Date	March 12, 1999
First Named Inventor	Karube
Examiner Name	Bronwen M. Loeb
Art Unit	1636

Attorney Docket No. 201487/1030

METHOD OF PAYMENT (check all that apply)

 Check Credit Card Money Order Other None
 Deposit Account:

Deposit Account Number

14-1138

Deposit Account Name

Nixon Peabody LLP

The Commissioner is authorized to: (check all that apply)

- Charge fee(s) indicated below Credit any overpayments
 Charge any additional fee(s)
 Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Fee (\$)	Small Entity Fee Code	Fee (\$)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	375
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) (\$375)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

Total Claims	-20** =	Extra Claims		Fee from below	Fee Paid
		0	X		
Independent Claims	2	-3** =	0	X	0
Multiple Dependent			X		0

Large Entity Fee Code	Fee (\$)	Small Entity Fee Code	Fee (\$)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) (\$0)

** or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity	Small Entity	Fee Description	
Fee Code	Fee (\$)	Fee Code	Fee (\$)
1051	130	2051	65
1052	50	2052	25
1053	130	1053	130
1812	2,520	1812	2,520
1804	920*	1804	920*
1805	1,840*	1805	1,840*
1251	110	2251	55
1252	410	2252	205
1253	930	2253	465
1254	1,450	2254	725
1255	1,970	2255	985
1401	320	2401	160
1402	320	2402	160
1403	280	2403	140
1451	1,510	1451	1,510
1452	110	2452	55
1453	1,300	2453	650
1501	1,300	2501	650
1502	470	2502	235
1503	630	2503	315
1460	130	1460	130
1807	50	1807	50
1806	180	1806	180
8021	40	8021	40
1809	750	2809	375
1810	750	2810	375
1801	750	2801	375
1802	900	1802	900
Other fee (specify) _____			

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) (\$985)

CERTIFICATE OF MAILING OR TRANSMISSION [37 CFR 1.8(a)]

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to Mail Stop _____, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, or being facsimile transmitted to the USPTO at _____, on _____

Signature: _____

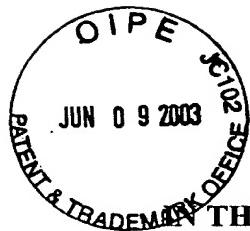
Name: _____

SUBMITTED BY

Complete (if applicable)

Name (Print/Type)	Michael L. Goldman	Registration No. (Attorney/Agent)	30,727	Telephone	(585) 263-1304
Signature	<i>Michael L. Goldman</i>			Date	<i>June 9, 2003</i>

SEND TO: Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450



Docket No.: 201487/1030 (SEN-002PCT-US)

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Karube et al.)	Examiner:
)	Bronwen M. Loeb
Serial No.	:	09/623,970)	Art Unit:
)	1636
Cnfrm. No.	:	1866)	
)	
Filed	:	March 12, 1999)	
)	
For	:	SITE-SPECIFIC CELL PERFORATION)	
		TECHNIQUE)	
)	

SECOND REQUEST FOR CORRECTED FILING RECEIPT

Mail Stop CPA
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

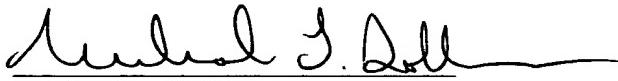
Applicants hereby request a corrected filing receipt for the above-identified application. On the enclosed copy of the official filing receipt, the entity status is still omitted. It should read "SMALL ENTITY". The statement for the small entity status claim is shown on the enclosed copy of the transmittal letter filed with the response to the Notification of Missing Requirements on December 21, 2000.

In addition, the title is still incorrect. The title reads "Site-specific cell perforation" but should read "Site-specific cell perforation technique". A copy of the first page of the specification as filed is enclosed herewith.

Since Applicants are not responsible for this error, no fee is enclosed.

Respectfully submitted,

Dated: June 9, 2003


Michael L. Goldman
Registration No. 30,727

Nixon Peabody LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603-1051
Telephone: (585) 263-1304
Facsimile: (585) 263-1600

RECEIVED
JUN 12 2003
TECH CENTER 1600/2900



UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
 UNITED STATES PATENT AND TRADEMARK OFFICE
 WASHINGTON, D.C. 20231
www.uspto.gov

APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	DRAWINGS	TOT CLAIMS	IND CLAIMS
09/623,970	12/28/2000	1632	970	201487/1030	13	20	2

CONFIRMATION NO. 1866

CORRECTED FILING RECEIPT



"OC000000006176571"



Michael L Goldman
 Nixon Peabody
 Clinton Square
 PO Box 31051
 Rochester, NY 14603

Date Mailed: 06/13/2001

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

Applicant(s)

Isao Karube, Kanagawa, JAPAN;
 Takashi Saitoh, Tokyo, JAPAN;

Domestic Priority data as claimed by applicant

THIS APPLICATION IS A 371 OF PCT/JP99/01223 03/12/1999

Foreign Applications

JAPAN 10/80177 03/12/1998

If Required, Foreign Filing License Granted 01/31/2001

Projected Publication Date: N/A

Non-Publication Request: No

Early Publication Request: No

* small entity

Title

Site-specific cell perforation

site-specific cell perforation technique

RECEIVED

JUN 12 2003

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ENTERED
Nixon Peabody LLP

JUN 20 2001

FILE 201487/1030
DKT JPB

**LICENSE FOR FOREIGN FILING UNDER
Title 35, United States Cod , Section 184
Title 37, Code f Federal Regulations, 5.11 & 5.15**

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Office of Export Administration, Department of Commerce (15 CFR 370.10 (j)); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15 (b).

PLEASE NOTE the following information about the Filing Receipt:

- The articles such as "a," "an" and "the" are not included as the first words in the title of an application. They are considered to be unnecessary to the understanding of the title.
- The words "new," "improved," "improvements in" or "relating to" are not included as first words in the title of an application because a patent application, by nature, is a new idea or improvement.
- The title may be truncated if it consists of more than 500 characters (letters and spaces combined).
- The docket number allows a maximum of 25 characters.
- If your application was submitted under 37 CFR 1.10, your filing date should be the "date in" found on the Express Mail label. If there is a discrepancy, you should submit a request for a corrected Filing Receipt along with a copy of the Express Mail label showing the "date in."
- The title is recorded in sentence case.

Any corrections that may need to be done to your Filing Receipt should be directed to:



- 1 -

SITE-SPECIFIC CELL PERFORATION TECHNIQUE

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JUN 12 2003

TECH CENTER 1600/2900

Technical Field

5 The present invention relates to a method for perforating a membrane by partially treating the membrane (cell membrane, etc.) with a membrane-denaturing agent, etc. It also relates to a membrane-disrupting material having a membrane-denaturing effect.

Background Art

10 In gene therapy and artificial substance production systems using living organisms, means of introducing a nucleic acid, a protein, and such, into the interior of a cell are extremely important. On the other hand, techniques for extracting structures such as the nucleus of a cell, are also gaining wide attention. In other words, 15 it can be said that injecting and extracting substances into/from cells, the basic unit constituting organisms, is a fundamental technique of bioengineering.

Conventional substance introduction techniques can be roughly categorized as follows:

- 20 a) Introduction techniques targeting non-specific cell groups
b) Introduction techniques targeting a specific cell

Examples of technique a) are, those using viral vectors (retroviral vectors, etc.), non-viral vectors (lipofectin, etc.), electroporation, calcium phosphate method, particle-gun method, etc.

25 Technique b) could be exemplified by the microinjection method ("Fundamental techniques of gene therapy", Youdosha (1995)).

Generally, technique b) is used against large cells, such as egg cells. One reason for this is that the microinjection method uses shear force of a capillary glass tube to disrupt the cell membrane, 30 and therefore, a technical limit probably arises due to the cell size. Also, this method requires skilled experience on the part of the handler, and therefore, automation is difficult. Furthermore, in many cases the pipette cannot be inserted due to the flexibility of the cell membrane of normal cells, except egg cells.

35 In technique a), a non-specific cell group is randomly treated, and it is hoped that the objective substance will be introduced to a part of the cell group. Therefore, very rarely does the objective



PATENT
Docket No.: 201487/1030 (SEN-002PCT-US)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Karube et al.

Serial No. : 09/623,970

Filed : March 12, 1999

For : SITE-SPECIFIC CELL PERFORATION TECHNIQUE

TRANSMITTAL LETTER

Assistant Commissioner For Patents
Washington, D.C. 20231
Box: PCT

Dear Sir:

In response to the Notification of Missing Requirements Under 35 U.S.C. 371, which was mailed by the United States Patent and Trademark Office on **October 23, 2000**, enclosed are:

- [X] A Request for One-Month Extension of Time.
- [X] A SIGNED Combined Declaration and Power of Attorney.
- [X] Applicants claim small entity status (See 37 CFR 1.27).
- [X] A copy of the Notification of Missing Requirements.
- [X] A self-addressed, prepaid postcard for acknowledging receipt.
- [X] Fees as calculated below:

FEE FOR ONE-MONTH EXTENSION OF TIME	\$55.00
TOTAL FEES SUBMITTED HEREWITH	\$55.00

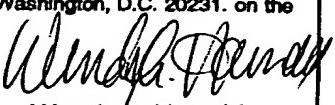
- [X] A check in the amount of **\$55.00** to cover the above fees.
- [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 14-1138. A duplicate copy of this sheet is enclosed.

Date: December 21, 2000


Edwin V. Merkel
Registration No. 40,087

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603
Telephone: (716) 263-1128
Facsimile: (716) 263-1600

R454661.1

Certificate of Mailing - 37 CFR 1.8 (a)	
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date below.	
12/21/00 Date	 Wendy L. Harrold